

AMENDMENT

Please amend the subject application as follows:

IN THE CLAIMS:

1. (Currently amended) A protein with beta-sheet structure and antibody-like binding activity towards a binding partner, wherein amino acids on a surface of the protein located in at least two β -strands of at least one beta sheet are mutagenized having the following locations:

- located in two, three or four beta-strands of at least one beta-sheet of said protein with beta-sheet structure;
 - said beta-sheet, said beta-strands and said amino acids are located on a surface of said protein, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the protein has a new or an improved antigen binding specificity, and wherein the protein to be mutagenized is selected from the group consisting of a crystallin, a spherulin, a heat shock protein, a cold shock protein, a β -helix protein, and a fibronectin, with the proviso that:
 - (i) the protein without substitution, deletion, ~~or~~ insertion, or combinations thereof has no binding activity[[,]] at the surface of the beta-sheet structure wherein the amino acids are mutagenized, and after substitution, deletion, ~~or~~ insertion, or combinations thereof at the surface of the beta-sheet structure, the protein has a new antibody-like antigen binding specificity; or
 - (ii) the protein has a binding activity before the substitution, deletion, ~~or~~ insertion, or combinations thereof, and that after the substitution, deletion, ~~or~~ insertion, or combinations thereof at the surface of the beta-sheet structure, the protein has an additional new or an improved antibody-like binding activity.
- 2-4. (Canceled)

5. (Previously presented) The protein of claim 1, wherein amino acids located in at least two beta strands of at least two beta sheets of the protein are mutagenized

6. (Previously Presented) The protein of claim 1, wherein amino acids located in three beta strands of two antiparallel beta sheets of the protein are mutagenized.

7. (Currently amended) The protein of claim 1, wherein the protein is a vertebrate gamma-crystallin.

8. (Previously presented) The protein of claim 1, wherein the protein is selected from the group consisting of an alpha-crystallin, a beta-crystallin, and a gamma-crystallin.

9. (Previously presented) The protein of claim 1, wherein the protein is a gamma-II-crystallin.

10. (Previously presented) The protein of claim 1, wherein an amino acid located within the protein is mutagenized in a region of the beta sheet that is accessible to a solvent.

11. (Previously presented) The protein of claim 1, wherein an amino acid is mutagenized in a region of the protein selected from the group consisting of a β -sheet structure of a domain of the protein and a β -sheet structure of a subunit of the protein.

12. (Previously presented) The protein of claim 9, wherein at least one of the amino acids Lys 3, Thr 5, Tyr 7, Cys 16, Glu 18, Ser 20, Arg 37, and Asp 39 of a bovine gamma-II-crystallin of SEQ ID NO: 22 is mutagenized.

13. (Canceled)

14. (Previously presented) The protein of Claim 1, wherein the new antigen binding specificity is for a compound selected from the group consisting of estradiol and BSA- β -estradiol-17-hemisuccinate.

15. (Previously presented) The protein of claim 1, wherein the protein has a new antigen binding specificity for a compound selected from the group consisting of estradiol and BSA- β -estradiol-17-hemisuccinate, and wherein the protein has an amino acid sequence comprising one of SEQ ID NO: 19 and SEQ ID NO: 21.

16. (Previously presented) A composition comprising the protein of claim 1 and at least one other protein or non-protein substance.

17. (Withdrawn) DNA coding for a protein according to claim 1.

18. (Withdrawn) RNA derived from the DNA according to claim 17.

19. (Cancelled)

20. (Withdrawn) Method for preparing the protein of claim 1, the method comprising:

- (a) mutagenizing a DNA coding for a protein with beta-sheet structure in those regions which code for at least two beta strands, exposed on the surface, of a beta sheet exposed on the surface;
- (b) expressing the DNA obtained in step (a) in an expression system to produce a protein encoded by the expressed DNA;
- (c) selecting a protein encoded by the expressed DNA having a desired property; and
- (d) isolating the protein encoded by the expressed DNA having the desired property.

21. (Withdrawn) Method according to Claim 20, wherein the mutagenizing comprises a site-specific substitution in the beta sheet.

22. (Withdrawn) Method according to claim 20, wherein the expressing is in a system selected from the group consisting of a prokaryotic cell, a eukaryotic cell, and a cell-free system.

23. (Withdrawn) Method according to claim 20, further comprising identifying a protein having a desired property by contacting the protein with a binding partner, wherein the binding of the protein to the binding partner identifies the protein as having the desired property.

24. (Withdrawn) Method according to claim 20, wherein the desired property of the protein is a catalytic activity and wherein identifying the protein having a desired catalytic activity comprises contacting the protein encoded by the expressed DNA with a substrate, wherein the binding of the protein encoded by the expressed DNA to the substrate identifies the protein encoded by the expressed DNA as having the desired catalytic activity.

25. (Withdrawn) A method of preparing a composition for use in an application selected from the group consisting of diagnostics, therapy, cosmetics, bioseparation, biosensors, and reducing harmful substances, the method comprising:

- (a) providing a protein according to claim 1; and
- (b) preparing a composition for use in an application selected from the group consisting of diagnostics, therapy, cosmetics, bioseparation, biosensors, and reducing harmful substances by incorporating therein the protein according to claim 1.

26. (Previously presented) The protein of claim 7, wherein the vertebrate is selected from the group consisting of a bovine, a rodent, a bird, and a fish.

27. (Previously presented) The protein of claim 1, wherein an amino acid of the protein is mutagenized in a region of the beta sheet that is accessible to a binding partner.

28. (Previously presented) The protein of claim 1, wherein an amino acid is mutagenized in a β -sheet structure of a subunit of the protein.

29. (Withdrawn) The method of claim 20, further comprising purifying the protein encoded by the expressed DNA.

30. (Withdrawn) The method of claim 20, wherein the expressing is on the surface of an entity selected from the group consisting of a plant cell, an animal cell, a yeast cell, a virus, and a bacterium.

31. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a site-specific deletion in the beta sheet.

32. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a site-specific insertion in the beta sheet.

33. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a random substitution in the beta sheet.

34. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a random deletion in the beta sheet.

35. (Withdrawn) The method according to Claim 20, wherein the mutagenizing comprises a random insertion in the beta sheet.

36. (Withdrawn) A vector comprising the DNA of claim 17.

37. (Withdrawn) The vector of claim 36, wherein the vector is a prokaryotic vector.

38. (Withdrawn) The vector of claim 36, wherein the vector is a eukaryotic vector.

39. (Withdrawn) The vector of claim 36, wherein the DNA has a nucleotide sequence that encodes a protein having an amino acid sequence that is one of SEQ ID NO: 19 and SEQ ID NO: 21.

40. (Withdrawn) A cell comprising the DNA of claim 17.

41. (Withdrawn) The cell of claim 40, wherein the DNA has a nucleotide sequence that encodes a protein having an amino acid sequence that is one of SEQ ID NO: 19 and SEQ ID NO: 21.

42. (Currently amended) A mutagenized gamma-crystallin polypeptide with antibody-like binding activity towards a binding partner, wherein amino acids on a surface of the gamma-crystallin polypeptide located in at least two β -strands of a least one beta sheet are mutagenized having the following locations:

- located in two, three, or for beta-strands of at least one beta-sheet of said gamma-crystallin polypeptide;
- said beta-sheet, said beta-strands and said amino acids are located on a surface of said protein, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the gamma-crystallin polypeptide has a new antibody-like antigen binding property specificity, with the proviso that:

- (i) the gamma-crystallin polypeptide without substitution, deletion, insertion, or combinations thereof has no binding activity at the surface of the beta-sheet structure wherein the amino acids are mutagenized, and after substitution, deletion, insertion, or combinations thereof at the surface of the beta-sheet structure, the gamma-crystallin polypeptide has a new antibody-like antigen binding specificity; or
- (ii) the gamma-crystallin polypeptide has a binding activity before the substitution, deletion, insertion, or combinations thereof and that

after the substitution, deletion, or insertion at the surface of the beta-sheet structure, the gamma-crystallin polypeptide has an additional new or an improved antibody-like binding activity

43. (Withdrawn) A method for preparing a gamma-crystalline ~~-crystallin~~ protein with a new binding property, the method comprising mutagenizing a gamma ~~crystalline -~~ crystallin polypeptide, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution and combinations thereof, to provide a mutagenized gamma ~~crystalline -~~ crystallin protein with a new binding property.

44. (Withdrawn) A method of preparing a protein with a new binding property, the method comprising:

- (a) mutagenizing a gamma ~~crystalline -~~ crystallin protein to provide a gamma ~~crystalline -~~ crystallin protein with a new binding property; and
- (b) combining the mutagenized gamma ~~crystalline -~~ crystallin protein with another protein to provide a protein with a new binding property.

45. (Withdrawn) The method according to claim 44, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution and combinations thereof.

46. (Currently Amended) A protein with beta-sheet structure and antibody-like binding activity towards a binding partner, wherein amino acids on a surface of the protein ~~located in at least two β -strands of at least one beta-sheet~~ are mutagenized having the following locations:

- located in two, three or four beta-strands of at least one beta-sheet of said protein with beta-sheet structure;
- said beta sheet, said beta-strands and said amino acids are located on a surface of said protein, wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof, such that the protein has a new or an improved antigen binding specificity and wherein the protein to be mutagenized is selected from the group consisting of a crystallin, a ~~spheruline~~ spherulin, a heat shock protein, a cold shock protein, a β -helix protein, and a fibronectin, with the proviso that:

- (i) the protein without substitution, deletion, or insertion, or combinations thereof has no binding activity at the surface of the beta-sheet structure wherein the amino acids are mutagenized, and after substitution, deletion, or insertion, or combinations thereof at the surface of the beta-sheet structure, the protein has a new antibody-like antigen binding specificity, or
- (ii) the protein has a binding activity before the substitution, deletion, or insertion, or combinations thereof, and that after the substitution, deletion, or insertion, or combinations thereof at the surface of the beta-sheet structure, the protein has an additional new or an improved antibody-like binding activity;

and further wherein said protein is prepared by a method comprising:

- (a) selecting a protein from the group consisting of a crystallin, spherulin, a heat shock protein, a cold shock protein, a β -helix protein, and fibronectin;
- (b) selecting a binding partner of the protein;
- (c) mutagenizing a nucleic acid molecule encoding amino acids on a surface of the protein said amino acids to be mutagenized having the following locations:
 - (i) located in two, three or four beta-strands of at least one beta-sheet of said protein with beta-sheet structure;
 - (ii) said beta-sheet, said beta-strands and said amino acids are located on a surface of said protein,~~located in at least two β strands of at least one beta-sheet of the protein with beta-sheet structure,~~ wherein the mutagenizing is selected from the group consisting of an insertion, a deletion, a substitution, and combinations thereof;
- (d) expressing the mutagenized nucleic acid molecule of step (c) in order to produce the mutagenized protein;
- (e) contacting the mutagenized protein with said binding partner of step (b); and
- (f) selecting and isolating of a mutagenized protein with a new or improved binding activity towards the binding partner of step (b).

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